Remarks

The Office Action mailed June 27, 2005 has been received and reviewed. Claims 1, 6, and 7 having been amended, claims 8 and 9 having been canceled, the pending claims are claims 1-7. Reconsideration and withdrawal of the rejections are respectfully requested.

Restriction Requirement

Applicants acknowledge the Examiner's reconsideration of the Restriction Requirement, mailed April 8, 2005, and thank the Examiner for the rejoinder and examination of SEQ ID NO:1-7 along with SEQ ID NO:8.

Objection to the Specification

The Examiner objected to the specification for containing a web site defined by a URL. Applicants submit that this objection to the disclosure is moot in view of the amendment of page 12, line 19 of the specification to remove the recitation of an URL identifier.

The 35 U.S.C. §112, First Paragraph, Rejection

The Examiner rejected claims 1-5 and 7 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is respectfully traversed.

Specifically, the Examiner asserted that while the specification is "enabling for a method of modulating an intracellular signaling molecule in a cell, the method comprising contacting the cell with an effective amount of colostrinin, a constituent peptide with a defined sequence (e.g., SEQ ID NO:1-8), or a combination thereof," the specification does not reasonably provide enablement for such a method "comprising contacting the cell with a modulator selected from the group consisting of a constituent peptide thereof, an active analog thereof, and combinations

thereof, where the structure of the constituent peptide or the active analog is not defined, and the components of the combinations are not defined" (page 4, Office Action mailed July 27, 2005).

Applicants submit that as amended, the structure of the constituent peptides of colostrinin and the active analogs of a constituent peptide of colostrinin in claims 1-5 and 7 are properly enabled. Specifically, the constituent peptides of colostrinin are selected from the group consisting of SEQ ID NO:1-8 and the active analogs of a constituent peptide of colostrinin have "an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to a constituent peptide of colostrinin selected from the group consisting of" SEQ ID NO:1-8. Applicants submit that the specification provides adequate instruction to allow one of skill to make and use the claimed constituent peptides of colostrinin and active analogs of constituent peptides of colostrinin. Applicants have provided the amino acid sequences of the constituent peptides of colostrinin (SEQ ID NOs:1-8) (see, for example, page 10, lines 5-10 of the specification), as well as guidance for active analogs of constituent peptides of colostrinin having an amino acid sequences with at least about 15 percent proline (see, for example, page 12, lines 9-14 of the specification), and having at least about 70 percent structural similarity to one of constituent peptides SEQ ID NOs:1-8) (see, for example, page 12, lines 29-33 of the specification). Applicants maintain it is routine for one of skill in the art to make and use the claimed constituent colostrinin peptides and active analogs thereof using the specification for guidance.

Further, the Examiner asserted that the specification "does not reasonably provide enablement for . . . a method of down regulating 4HNE-mediated lipid peroxidation in a cell" (see page 4, Office Action mailed June 27, 2005), as claimed in claim 7. In support of this assertion, the Examiner stated that "there are no working examples indicating 4HNE-mediated lipid peroxidation is down regulated by colostrinin, constituent peptides thereof, or the active analogs thereof in a cell" (see page 6, Office Action mailed June 27, 2005). Applicants respectfully disagree. To clarify the claimed invention, claim 7 has been amended to recite a "method of down regulating the 4-hydroxynonenal (4HNE)-mediated oxidative damage

associated with lipid peroxidation in a cell." As explained in the specification, 4HNE is a 3'-unsaturated aldehyde generated endogenously during lipid peroxidation in a cell (page 23, lines 8-9 of the specification). Further, Applicants direct the Examiner to Example 2, (see page 18, line 30 to page 19, line 8; page 20, line 30 to page 21, line 17; and page 23, lines 6-11 of the specification) demonstrating the protective effects of colostrinin, constituent peptides, or an active analog thereof against the oxidative damage induced of 4HNE exposure. Thus, Applicants submit that the specification provides adequate instruction to allow one of skill in the relevant art to practice the claimed method of down regulating the 4HNE-mediated oxidative damage associated with lipid peroxidation in a cell.

Applicants respectfully submit that the specification provides adequate instruction to allow one of skill in the relevant art to make and use the invention commensurate with the scope of claims 1-5 and 7. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, are respectfully requested.

The 35 U.S.C. §112, Second Paragraph, Rejection

The Examiner rejected claims 1-7 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed.

Specifically, the Examiner asserted that the recitation "combinations thereof" is indefinite, as "it is not clear what components and how much of each component are included in the combinations since the identities of the constituent peptides of colostrinin and/or the active analogs are not indicated in the claim" (pages 8 of Office Action mailed June 27, 2005). Applicants respectfully disagree and submit that the recitation "and combinations thereof" in claims 1, 6, and 7 is not indefinite. Each claim utilizes traditional Markush group format; members "being selected from the group consisting of A, B and C." See MPEP § 2173.05(h). For example, claim 1 is drawn to "a modulator selected from the group consisting of colostrinin, a constituent peptide of colostrinin, an active analog of a constituent peptide of colostrinin, and

combinations thereof." The elements of the Markush group recited in claim 1 are colostrinin, constituent peptides of colostrinin, active analogs of constituent peptides of colostrinin, and each of the various combinations thereof. Applicants submit that the metes and bounds of the claim are clear to one of skill in the art and the recitation "combinations thereof" is not indefinite.

Further, the Examiner asserted that claims 1-7 are indefinite in the recitation of the abbreviation "4HNE." Applicants submit that this rejection is moot in view of the amendment of claims 1 and 7 to recite "4-hydroxynonenal" along with the first recitation of the abbreviation 4HNE in each of independent claims 1 and 7. Applicants submit that no new matter is introduced with this amendment, as 4HNE is the well known and accepted abbreviation for 4-hydroxynonenal, as shown, for example, by Bruce-Keller et al., J Neuropathol Exp Neurol, 1998;57:257-267 (see abstract); Cheng et al., Arch Biochem Biophys, 1999;372:29-36 (see abstract); Esterbauer et al. Free Radic Biol Med. 1991;11(1):81-128 (see page 81, bottom of column 2); Kruman et al., J Neurosci, 1997;17:5089-5100 (see abstract); Lovell et al., Neurobiol Aging. 1997 18(5):457-61 (see abstract); Page et al., J Biol Chem, 1999;274:11611-11618 (see abstrct); Poli et al., IUBMB Life, 2000;50:315-321 (see abstract); and Sayre et al., J Neurochem, 1997;68:2092-2097 (see abstract). Applicants note that copies of each of Bruce-Keller et al., Cheng et al., Esterbauer et al. (cited on page 23, lines 8-12 of the specification), Kruman et al., Lovell et al., Page et al., Poli et al., and Sayre et al. were provided with the Information Disclosure Statement filed on November 11, 2004.

Finally, the Examiner asserted that claims 1-7 are indefinite because the claims "lack an essential step in the method of modulating an intracellular signaling molecule or down regulating 4HNE-mediated lipid peroxidation in a cell. The missing step is an effective amount of modulator used (for claims 1-7) and the outcome of the treatment (for claim 7)" (page 9 of Office Action mailed June 27, 2005). Applicants respectfully submit that this rejection is moot in view of amendments to claims 1 and 7. To clarify the claimed invention, claims 1 and 7 have been amended to recite "in an effective amount," and claim 7 has been amended to recite "and

wherein the 4HNE-mediated oxidative damage associated with lipid peroxidation in a cell is down regulated."

In view of the above discussion, reconsideration and withdrawal of this rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

Summary

It is respectfully submitted that the pending claims 1-7 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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The undersigned hereby certifies that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to **Mail Stop Amendment**, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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